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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/975,881	10/12/2001	Valentin K. Gribkoff	CT-2590-NP	9722

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EXAMINER

STOCKTON, LAURA LYNNE

ART UNIT PAPER NUMBER

1626

DATE MAILED: 11/19/2002

8

Please find below and/or attached an Office communication concerning this application or proceeding.



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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on August 22, 2002

☐ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), ~~within 60 days~~, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- ☒ Claim(s) 1-65 are pending in the application.
Of the above, claim(s) 46-65 are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 1-45 are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) _____
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

- ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☒ Notice of Reference Cited, PTO-892
- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 2
- ☐ Interview Summary, PTO-413
- ☒ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

DETAILED ACTION

Claims 1-65 are pending in the application.

Election/Restrictions

Applicants' election with traverse of Group I in Paper Nos. 5 and 7 and the species found in claim 10 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that Groups I and II should be combined because Groups I and II are drawn to methods, both groups are classified in class 514 and claim 14, and dependent claims included in Group II, could be classified as a subgenus of claim 1.

In response, the Examiner agrees to combine the inventions of Groups I and II with the understanding that all non-elected inventions be cancelled when responding to this Office Action.

The requirement is still deemed proper and is therefore made
FINAL.

Claims 46-65 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions. Applicant timely traversed the restriction (election) requirement in Paper Nos. 5 and 7.

It is suggested that in order to advance prosecution, the non-elected subject matter be cancelled when responding to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C.

112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 12-15, 19-23, 28-37, 41 and 43-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific fluoro-oxindole and chloro-oxindole compounds

disclosed (see, for example, claims 9 and 11), but does not reasonably provide enablement for all maxi-K potassium channel openers known to man at present or those which may be discovered in the future. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, Applicants claim a method of treating a disease or disorder characterized by high intracellular calcium levels comprising providing an effective amount of an opener of maxi-K potassium channels. Applicants also claim a method of treating stroke comprising administering a maxi-K channel opener. The nature of the pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant specification does not give any guidance as to the full range of openers of maxi-K potassium channels that could be used to treat a disease or disorder using the instant claimed process. In order to practice the claimed invention, one skilled in the art would have to speculate which compounds could be used to treat a disease or disorder

found in the instant claims. The number of possible compounds that could be embraced by the claims that would have to be tested would impose undue experimentation on the skilled art worker. Therefore, the broad terminology "an opener of maxi-K potassium channels" is not enabled because the metes and bounds of compounds that could be used to treat a disease or disorder in the instant claims cannot be ascertained.

This rejection may be overcome by adding the specific fluoro-oxindole and chloro-oxindole compounds (e.g. see instant claims 9, 11, 16, 18 and 42) to independent claims 1, 14, 22, 35 and 36.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-10, 12-17, 19-26, 28-37 and 43-45 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 23, 24 and 28-31 of U.S. Patent No. 5,565,483 and over claims 5-10 of U.S. Patent No. 5,602,169. Although the conflicting claims are not identical, they are not patentably distinct from each other because there is an overlap between the subject matter in the instant claims and the subject matter embraced by the claims in the patents.

Claim 23 in U.S. Pat. 5,565,483 claims a method for the treatment of disorders responsive to opening of the large conductance calcium-activated potassium channels (also known as maxi-K channels) by administering a therapeutically effective amount of a compound in claim 1. Claim 1 of the patent embraces fluoro-oxindole compounds. Also see

claim 31 in the patent and the third compound listed in claim 21 of the patent.

Claim 5 in U.S. Pat. 5,602,169 claims a method for the treatment of disorders responsive to opening of the large conductance calcium-activated potassium channels (also known as maxi-K channels) by administering a therapeutically effective amount of a compound in claim 1. Claim 1 of the patent is the same compound listed in instant claim 10 (which is also the elected species).

One skilled in the art would thus be motivated to prepare products embraced by the patents to arrive at the instant claimed invention with the expectation of obtaining products which would be useful in treating disorders such as stroke, traumatic brain injury, etc. Therefore, the instant claimed invention would have been suggested to one skilled in the art.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-10, 12-17, 19-26, 28-40 and 43-45 are rejected under 35 U.S.C. 102(b) as being anticipated by Hewawasam et al. {U.S. Pat. 5,565,483} and Hewawasam et al. {U.S. Pat. 5,602,169}.

Hewawasam et al. '483 disclose Example 14 that is an opener of the large-conductance calcium-activated potassium channels (also known as maxi-K channels) and is useful in the treating of disorders (e.g., ischemic stroke, traumatic brain injury, etc.) which are responsive to the opening of the potassium channels (column 1, lines 5-13, 31-33 and 47-53; column 13, lines 41-53; and column 25, lines 40-52).

Hewawasam et al. '169 disclose Examples 14, 37 and 38 which are openers of the large-conductance calcium-activated potassium channels and are useful in the treating of disorders (e.g., ischemic stroke, traumatic brain injury, etc.) which are responsive to the opening of the potassium channels (column 1, lines 12-19, 37-39 and 53-59; column 3, lines 23-63; column 13, lines 41-53; and column 26, lines 36-51; column 31, lines 26-56).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hewawasam et al. {U.S. Pat. 5,565,483} and Hewawasam et al. {U.S. Pat. 5,602,169}.

Determination of the scope and content of the prior art (MPEP §2141.01)

Applicants claim a method of treating a disease or disorder characterized by high intracellular calcium levels comprising providing an effective amount of an opener of maxi-K potassium channels (e.g. fluoro-oxindole and chloro-oxindole compounds). Each of Hewawasam et al. '483 (column 1, lines 5-13, 31-33 and 47-53; column 13, lines 19-53; and column 25, lines 40-52) and Hewawasam et al. '169 (column 1, lines 12-19; column 3, lines 23-63; column 13, lines 19-53; Example 14 in column 26, lines 36-51; and Example 37 and 38 in column 31, lines 26-56) teach fluoro-oxindole compounds, which are openers of the large-conductance calcium-activated potassium channels (also known as maxi-K channels) and are useful in the treating of disorders (e.g. ischemic stroke, traumatic brain injury, etc.) which are responsive to the opening of the potassium channels.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between some of the products taught by the Hewawasam et al. references and the products instantly claimed is that of generic description (e.g., see instant claim 8).

The difference between some of the products taught by the Hewawasam et al. references and the products instantly claimed (e.g., see instant claim 11) is that of fluoro-oxindole instead of chloro-oxindole.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

The indiscriminate selection of “some” among “many” is *prima facie* obvious. The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g., an opener of maxi-K channels).

In Ex parte Wiseman, 98 USPQ 277 (1953), it was held that compounds are rejected over prior art when the difference between the claimed compounds and the compounds of the prior art is two fluorine atoms versus chlorine atoms. The basis of this reasoning is that fluorine and chlorine are both halogen elements from the seventh group of the

periodic system and the claimed compound is thus an analogue or an isologue of that disclosed in the prior art. The compounds are expected to possess similar properties differing only in degree.

One skilled in the art would thus be motivated to prepare products embraced by the Hewawasam et al. references, or alternatively, prepare the chloro-oxindole products instead of the fluoro-oxindole products, to arrive at the instant claimed invention with the expectation of obtaining products which would be useful in treating disorders such as stroke, traumatic brain injury, etc. Therefore, the instant claimed invention would have been suggested to one skilled in the art.

The method of using the elected species of instant claim 10 is not allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to

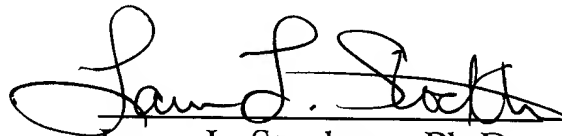
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Laura L. Stockton whose telephone number is (703) 308-1875. The examiner can normally be reached on Monday-Friday from 6:00 am to 2:30 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (703) 308-4537.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

A handwritten signature in black ink, appearing to read "Laura L. Stockton", written over a horizontal line.

Laura L. Stockton, Ph.D.

Patent Examiner

Art Unit 1626, Group 1620

Technology Center 1600

November 15, 2002